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Palladium-Catalyzed Intramolecular Addition of Trisilanes to Carbon-Carbon Double Bonds. Polyol Synthesis by Use of a Disilanyl Group as a Hydroxyl Equivalent.

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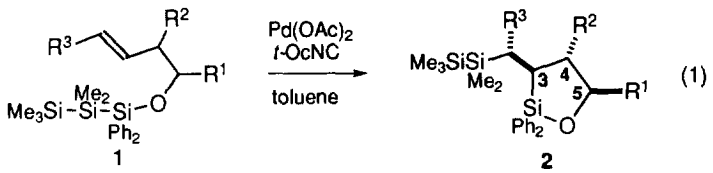
Abstract: Intramolecular cyclization of trisilanyl ethers of homoallylalcohols proceeded regio- and stereoselectively with a 5-exo mode to give 3-(disilanylmethyl)-2-silatetrahydrofuran derivatives in good yields in the presence of a *t*-alkyl isonitrile–palladium catalyst. From the cyclized products thus obtained were synthesized polyols including the key intermediate in the total synthesis of (–)-avenaciolide via stepwise oxidation of the silyl and disilanyl groups.

We recently reported that a disilanyl group serves as a synthetic equivalent of the hydroxy group in organic synthesis.[1,2] The new hydroxyl equivalent features high stability toward some typical reagents employed for organic synthesis, e.g., Lewis acids, alkylmetals, and metal hydrides. Furthermore, the disilanyl group is readily converted into the hydroxyl group by a simple one-pot procedure involving a cleavage of the Si–Si bond by tetrabutylammonium fluoride (TBAF) and subsequent oxidation with basic hydrogen peroxide. The usefulness of the hydroxyl equivalent will surely be enhanced by development of effective methods for the synthesis of disilanyl compounds.

We have developed stereoselective intramolecular bis-silylation reactions of carbon-carbon double bonds catalyzed by *t*-alkyl isonitrile–palladium(0) complexes.[3] The two vicinal organosilyl groups thus introduced were successfully transformed into 1,2-hydroxyls to lead to the stereoselective synthesis of polyols. Herein, we disclose the regioselective introduction of a disilanyl group and a silyl group in a vicinal fashion into an alkene by palladium-catalyzed intramolecular addition of a trisilane to a carbon-carbon double bond. Difference in reactivity between the silyl and the disilanyl groups made their stepwise oxidation possible, leading to straightforward synthesis of acetonide-protected polyols without use of tentative protective groups, which would be usually required for the selective reaction of hydroxyls.

Trisilanyl ethers of homoallylic alcohols **1a-e** were prepared by the reaction of 1-chloro-1,1-diphenylpentamethyltrisilane[4] with the corresponding alcohols in good yields. Intramolecular disilanyl–silylation (eq 1) of **1a-e** thus prepared were carried out in the presence of a catalyst prepared from $Pd(OAc)_2$ (2 mol%) and 1,1,3,3-tetramethylbutyl isocyanide (30 mol%) in toluene (Table 1). The reactions of terminal



1 **2** (1)

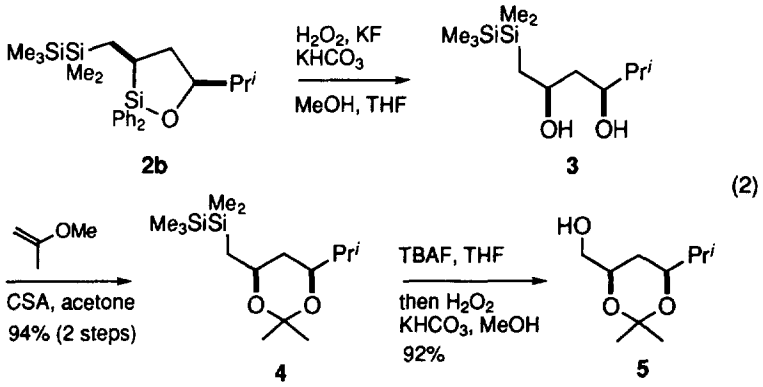
Table 1. Palladium–Catalyzed Intramolecular Disilanyl-Silylation of Alkenes[a]

entry	1	R^1	R^2	R^3	2 (yield / %)	*cis* : *trans* (position)
1[b]	a	Me	H	H	a (91)	>95:<5 (3,5)
2[b]	b	Pr^i	H	H	b (98)	>95:<5 (3,5)
3[b]	c	H	Me	H	c (93)	<5:>95 (3,4)
4[c]	d	H	H	Et	d (61)	——
5[c]	e	Me	H	Et	e (84)	9:1 (3,5)

[a]$Pd(OAc)_2$ (0.02 eq), 1,1,3,3-tetramethylbutyl isocyanide (0.30 eq).
[b]Reaction at room temperature. [c]Reaction at 80°C.

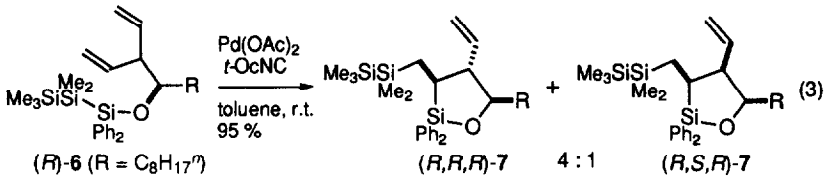
alkenes smoothly proceeded at room temperature (entries 1–3), while 80°C was required for the reactions of internal alkenes (entries 4 and 5). Noteworthy was that 5-exo ring closure products, which were formed through selective addition of the Si–Si bond proximal to the oxygen atom to the carbon-carbon double bond, were exclusively obtained without formation of 6-exo products. The regioselective disilanyl-silylation also proceeded with high diastereoselectivity as well as stereospecific *cis* addition as we previously reported for the bis-silylation reactions using disilanyl ethers. Thus, ethers **1a**, **b**, and **e** with substituents β to the double bonds gave 3,5-*cis* products (entries 1, 2 and 5) and that with an α substituent gave a 3,4-*trans* product (entry 3) in high yields.

The Si–C bond bearing at least one hetero substituent on the silicon atom is oxidized with hydrogen peroxide in the presence of fluoride anion to give the corresponding alcohols with retention of the stereochemistry at the carbon atom.[5] Treatment of **2b** with basic hydrogen peroxide in the presence of potassium fluoride gave diol **3** in high yield by selective oxidation of the ring Si–C bond (eq 2). The disilanyl



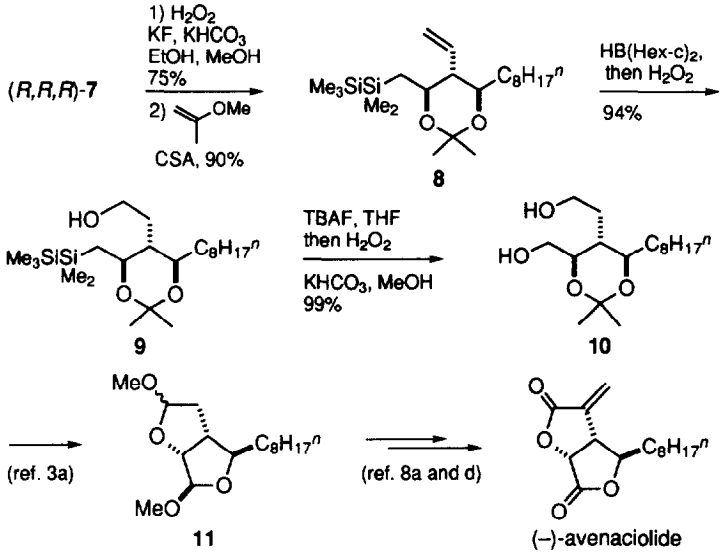
group remained intact under this reaction condition. Subsequent protection with acetonide afforded **4** in 94% yield for the two steps. Disilane **4** was then subjected to the oxidation reaction according to the procedure reported previously, i.e., treatment with 2 equiv of TBAF for 10 min. followed by addition of excess H_2O_2, to give alcohol **5** in high yield. Neither Peterson elimination[6] nor homo Brook rearrangement,[7] which would result in a loss of the disilanyl group, occurred during the oxidative transformation.

A synthetic usefulness of the disilanyl group as the hydroxyl equivalent was demonstrated by a short total synthesis of natural antifungal metabolite (–)-avenaciolide.[8] We have recently reported that intramolecular bis-silylation of (*R*)-3-vinyl-1-dodecen-4-ol proceeded with high diastereoselectivity, ultimately leading to the synthesis of (–)-avenaciolide.[3a] Unlike the multistep total synthesis of the (–)-avenaciolide based on the bis-silylation, the disilanyl–silylation procedure did not require any tentative protection of the resultant hydroxy groups in the synthetic route to acetonide-diol **10**. Trisilanyl ether (*R*)-**6** (98% ee)[9] underwent the intramolecular disilanyl-silylation at room temperature to give 5-membered product **7** in good yield (eq 3).



(*R*)-**6** (R = $C_8H_{17}^n$) (*R,R,R*)-**7** (*R,S,R*)-**7**

Only two of the four possible diastereomers were formed in a ratio of 4 : 1, which were separated by HPLC to afford the major isomer (*R,R,R*)-**7**. Selective oxidation of the ring Si–C bond was effected by H_2O_2 / KF / $KHCO_3$ at room temperature to give a diol, whose hydroxyl groups were protected by an acetonide to afford **8** (Scheme 1). Hydroboration with dicyclohexylborane followed by basic hydrogen peroxide oxidation gave alcohol **9** in good yield. Finally, conversion of the disilanyl group to the hydroxyl group was successfully carried out by the treatment with TBAF and H_2O_2 to give acetonide-diol **10** quantitatively. We have already reported the synthesis of (–)-avenaciolide from **10**.[3a] Thus, bis-lactol **11** was prepared in high yield by Swern oxidation of the two primary hydroxyls and subsequent acidic deprotection of an acetonide in methanol. Treatment of **11** with *m*-chloroperbenzoic acid in the presence of boron trifluoride etherate gave a bis-lactone,[8d] which was finally methylenated to give (–)-avenaciolide.[8a] The stereocontrolled total synthesis of (–)-



Scheme 1. Formal Total Synthesis of (–)-Avenaciolide.

avenaciolide consisting of only ten steps from nonanal demonstrated the synthetic usefulness of the palladium-catalyzed disilanyl-silylation.

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9. (*R*)-3-Vinyl-1-dodecen-4-ol with 98% ee was prepared by enantioselective γ-pentadienylation of nonanal. See ref 3a.

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